Amendments to the Specification:

Please replace the first full paragraph on page 14 (lines 14-20) with the following amended paragraph:

Polymers of the invention are naturally derived polymers, such as albumin, alginate, cellulose derivatives, collagen, fibrin, gelatin, and polysaccharides as well as synthetic polymers such as polyesters (PLA, PLGA), polyethylene glycol, poloxomers, polyanhydrides, polyorthoesters, polyanhydrides, polyurethanes, and pluronics. Polymers are designed to be flexible; the distance between the bioactive sidechains and the length of a linker between the polymer backbone and the group can be controlled. ~~Other suitable polymers and methods for their preparation are described in U.S. Pat. Nos. 5,455,044 and 5,576,018~~.

Please replace the third full paragraph on page 32 (lines 20-30) with the following amended paragraph:

The size of microspheres is determined using microscopy techniques. High performance liquid chromatography (HPLC) is used to quantify and determine release profiles. 5 ml of 10 mM PBS was added to PLGA/Inosine microspheres, that were manufactured using either ethyl acetate or methylene chloride as the solvent. After about 3 hours, 4 mL of PBS was drawn off the sample and replaced with 4 mL of fresh PBS. This procedure was repeated at the end of each time interval. Inosine concentration for the 4 mL aliquot of PBS was determined by HPLC analysis. The cumulative amounts of inosine released over 10 days and release profiles are found in Fig. 10. Results indicate that for microspheres manufactured using ethyl Acetate, 23.8% of the total inosine was released over 10 days. Microspheres manufactured using methylene chloride~~Chloride~~ had about 44.2% of total inosine released over the 10 day period.

Please replace the second full paragraph on page 39 (lines 20-29) with the following amended paragraph:

Male Sprague-Dawley rats (300-350 g) are anesthetized with either an intramuscular injection of ~~Chloral Hydrate 4mg/kg~~ chloral hydrate 4 mg/kg or a ketamine, xylazine and acepromazine cocktail. The head is shaved then prepped and mounted in a stereotaxic frame.

Body temperature is maintained at 37 ± 0.5° C during the procedure using a heating blanket connected to a temperature controller. A midline incision centered over the left parietal cortex is performed. When the skull dries, suture lines appear. A 2 mm~~2mm~~-diameter craniotomy is made at the level of the right parietal cortex (3.5mm anterior to, 6mm above the interaural line); the dura is left intact at this opening. A 2.0mm hollow female Leur-Loc placed over the dura is fitted to the craniectomy site and anchored to the skull using dental cement.

Please replace the paragraph on page 15, line 27- page 16, line 9 with the following amended paragraph:

In a preferred embodiment, the polymer used is a poly(lactide-co-glycolide) copolymer (PLGA). The Food and Drug Administration has approved products made of PLGA (i.e. LUPRON DEPOT®, leuprolide acetate for depot suspension~~Lupron Depot®~~). Even more importantly, PLGA has shown to be non-toxic when placed in the CNS. PLGA is soluble in organic solvents. PLGA degrades by bulk hydrolysis in water as a function of the lactide:glycolide ratio and molecular weight (Langer R. et al., Chemical and physical structure of polymers as carriers for controlled release of therapeutic agents: a review, *JMS-Rev. Macromol. Chem. Phys.*, 23: 61 – 126, 1983; Gopferich A., Polymer bulk erosion., *Macromolecules* 30: 2598-2604, 1997.) The rate of PLGA hydrolysis controls the rate of release of an encapsulated pharmaceutical. Thus, one can control the release of a drug in a PLGA polymer matrix by varying PLGA's lactide:glycolide ratio and molecular weight. Also, by controlling various process parameters (*i.e.* solvent/non-solvent systems, shear rate during emulsification or hardening) it is possible to control the size of the microspheres made from the PLGA/drug matrix.

Please replace the paragraph on page 15, lines 11-14 with the following amended paragraph:

Non-Volatile Oils: mineral oil~~Mineral Oil~~, isopropyl myrisate~~Isopropyl Myrisate~~, LIBRAFIL 1944™ (oleoyl macrogol-6 glycerides)~~Librafil™ 1944~~, vegetable oil~~Vegetable Oil~~, glyceryl monostearate~~Glycerl Monostearate~~, parrafin~~Parrafin~~, oelic acid~~Oelic Acid~~, methyl oelate~~Methyl Oelate~~, lanolin~~Lanolin~~, petrolatin~~Petrolatin~~, cetyl alcohol~~Cetyl Alcohol~~, fish oil, corn oil~~Corn~~

~~Oil~~, soybean oil~~Soybean Oil~~, vitamin E~~Vitamin E~~, polyalkyleneglycol such as polyethyleneglycol of various molecular weights, and castor oil~~Castor Oil~~.

Please replace the paragraph on page 31, line 26-page 32, line 10 with the following amended paragraph:

Specifically, in a preferred embodiment, a method for manufacturing polymer microspheres comprising at least one therapeutic agent and at least one buoyancy agent comprises the steps of: milling and/or sieving the therapeutic agent to the desired size range (about 5 μm or less), dissolving the polymer solution in methylene chloride, or another suitable solvent, (to make a 10% polymer/solvent solution), dispersing the therapeutic agent (*e.g.*, Inosine) in polymer solution by stirring and/or shaking, stirring the agent/polymer solution while adding silicone oil to create an emulsion, slowly (drop wise) adding the emulsion to hexane containing 0.5% w/w ~~Span~~ SPAN® 85 (sorbitan trioleate) that is being stirred rapidly and being sonicated by a sonic dismembrator, adding the appropriate amount of buoyancy agent, by mixing and/or agitating in a way to achieve desired buoyancy, briefly sonciating and stirring for 20 minutes. The spheres are then left to settle for about 5 minutes after which the excess hexane is sucked off. Then 0.5% ~~Span 85~~SPAN® 85 (sorbitan trioleate) -hexane solution is added bringing the total volume to 500 ml. The microspheres are re-suspended, briefly sonicated and stirred for 20 minutes. This process of settling and adding is repeated a few times until the desired range of sizes of microspheres is achieved. The microspheres are then vacuum dried overnight.

Please replace the paragraphs on page 33, lines 18-31 with the following amended paragraphs:

Animals are fasted from solid food for twelve hours prior to the study. Animals are pre-medicated with 6 mg/kg xylazine (2-(2,6-Dimethylphenylamino)- 5,6-dihydro-4H-thiazine) ~~Xylazine~~, sq., and are anesthetized with a mixture of xylazine~~Xylazine~~, 10 mg/ml, and ketamine~~Ketamine~~, 40 mg/ml, iv to effect. They are then intubated and transitioned to inhalation anesthesia, 1-2% halothane~~Halothane~~ in ~~02/N2O~~O_2/N_2O, 2/1, for the duration of the study.

Various routes of administration are tested. Among these various routes are intraventricular administration. Under sterile conditions, the scalp is opened in the midline and

the skin and underlying muscle reflected laterally to expose the skull. Under stereotactic guidance a neurosurgical burr is used to remove a small amount of skull bone and expose the dura. Then, under stereotactic control, a catheter is introduced into the area of interest, the lateral ventricle, both ventricles, and/or the subarachnoid space(s). Drug is then infused in various doses into the areas of interest. Animals to be recovered will have the hole in the skull packed with sterile ~~Gelfoam~~GELFOAM® (absorbable gelatin), the muscles of the scalp closed in layers, and the skin closed with a running subcuticular suture.

Please replace the paragraph on page 35, lines 29-30 with the following amended paragraph:

Using the ~~Image Pro-Plus~~ IMAGE PRO-PLUS® (scientific image processing and analysis software from Media Cybernetics), a total of 14 images per brain of both the frontal and posterior side of each slice are analyzed through digital analysis.